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Formulation and Evaluation of Nail Lacquer Containing Anti fungal Griseofulvin for the Treatment of Onychomycosis

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Abstract:- Onychomycosis is a fungus that infects the human nail and affects 19% of the world's population. It is responsible for half of all nail problems in diabetic and older individuals. Dermatophytes are the most frequent cause of onychomycosis, although yeasts and candida may also cause it, because the illness is persistent, difficult to eliminate, and prone to recurrence, it is tough to control. The diseased nails are unsightly, discoloured, thicker, and dystrophic, which has a detrimental effect on the patient's social life.

Topical therapy has been shown to be a viable alternative to systemic administration in the treatment of onychomycosis, since it is capable of overcoming many of the constraints of systemic administration and targeting the medication at its site of action with minimal interactions and side effects. Limited permeability of the medication through the nail plate and blood supply in the afflicted region may result in sub-therapeutic concentrations, which may be addressed by applying the drug topically. Furthermore, since most commonly used formulations are easily removed by rubbing or washing, they are not particularly suited to the nail. To get over these obstacles, ungual delivery (drug administration across the nail plate) may be used.

Transungual drug delivery is a method for transporting drugs through the nail to provide targeted medication administration in the treatment of nail disorders. "Trans" means "through", and "unguis" means "nails" in the word transungual [10]. Because of its superior adherence and localised action, which offers less systemic adverse effects, the transungual medication delivery method is considered to be highly useful in managing nail diseases.

Nail lacquers seem to be commercially preferred for a variety of reasons, including their long residence duration on the nail plate and low wash-off or loss resistance. Nail lacquers are also generally accepted by patients and simple to apply, in addition to preventing tranonychial water loss and allowing for prolonged medication diffusion through concentration gradients.

I. INTRODUCTION

Disease by species of the genus *Epidermophyton, Trichophyton, Microsporum,*& is referred to as "dermatophytosis." *T. rubrum, T. mentagrophytes,* and *Epidermophyton floccosum*are very much common species which induce onychomycosis in North America & portion of Europe; the initial two species are considerably more frequently associated with *E. floccosum.* Dermatomycoses are diseases of the hair, dermis & nails caused by non-dermatophytic moulds such as *Scopulariopsis*& *Scytalidium.* Dermatophytes are responsible for the majority of toenail onychomycosis (90percent) & at least half of nail disease [1]. Onychomycosis is induced by non dermatophytes& dermatophytes, particularly *C. albicans*; but the frequency of genuine mixed disease (induced by non-dermatophytes & dermatophytes) is hard to estimate exactly [2].

Hyaline septate moulds make up the dermatophytes. This mycelial species' hyphae enter the nail's & skin's stratum corneum. Keratinolytic proteases are produced by cells of fungus and offer a pathway inside live tissues [3]. Some dermatophytic species, which are essentially soil saprophytes with the capacity to breakdown keratinous detritus in soil, has adapted to parasitize keratinous cells of animals [4].

Among the most prevalent dermatological diseases is onychomycosis. In the United Kingdom, a comprehensive questionnaire study of 10,000 individuals revealed a frequency of 27.1 percent [5, 6]. Current mycologically observational trials in Finland [7] & the United States [8] suggest a frequency of ten- seven percent. Increased awareness of infectious diseases, as well as the introduction of better new antifungal medications, has resulted in a higher desire amongst patients to receive therapy & among doctors to prescribe therapy. Medication is frequently recommended without mycological verification of disease; there might be some uncertainty about whether fungi isolated on culture are secondary or primary pathogens; the relative efficacy of different antifungal agents against different fungi is not completely accepted; & medicines are frequently recommended for insufficient durations of therapy.

II. MATERIAL

A. Drug and Excipients used in the formulation

Siemen Laboratories sent a free sample of griseofulvin (Gurgaon, India). Evonik Roehm Pharma polymers provided Eudragit RS 100. (Essen, Germany). Hi media Labs Ltd provided the thioglycolic acid (TGA) (Mumbai, India). K. M. Chem Ltd provided the menthol (Mumbai, India). SD-Fine Chem Ltd provided the nbutanol (Mumbai, India). SD-Fine Chem Ltd provided the isopropyl alcohol (Mumbai, India).

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Sigma Aldrich Ltd provided the polyethylene glycol 400. (U.S.A). SD-Fine Chem Ltd provided the glycerol (Mumbai, India).

III. METHODS

A. Solvent system for optimization

To obtain the best drying time for the nail lacquer film, the solvent system was optimised. By changing the ratio of isopropyl alcohol and n-butanol in the solvent system, 4 blank formulations were created. PEG 400, glycerol (plasticizers), and Eudragit RS 100 (film forming agent) concentrations were held constant. On glass petridish, a 4.0x4.5 cm^2 area was defined, and a homogeneous coating of formulation (0.2 mL) was applied with a nail lacquer brush. The drying time of the formulation(s) was calculated, and the solvent system with the shortest drying time was chosen.

Selection of optimum ratio of desired solvent system								
Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Eudragit RS 100 (% w/v)	10	10	10	10	10	10	10	10
PEG 400 (% v/v)	10	10	10	10	10	10	10	10
Glycerol (% v/v)	10	10	10	10	10	10	10	10
n- Butanol : Isopropyl alcohol (ml)	1:1	1:2	1:5	1:6	1:4	1:5	1:6	1:4
Drying time (sec)	120	70	66	45	54	65	60	70

Table : 1

B. Nail Lacquer preparation

The experimental nail lacquers were made by dissolving a suitable quantity of griseofulvin in a base lacquer comprising butyl acetate, ethanol (96%), triacetin, ethyl acetate, and one of the film-forming polymers Eudragit RS100, ethyl cellulose, and Eudragit RL100. Table 3.2 shows eight formulations with 1 percent griseofulvin nail lacquers as experimental compositions:

Full-Factorial design for the preparation of tolnaftate based nail lacquer							
Formulation Code	Griseofulvin (% w/v)	TGA (% w/v) X_1	Eudragit (% w/v) X_2	PEG (% w/v)	Glycerol (% w/v)	Menthol (%w/v)	n-butanol: IPA
F1	1	10 (+)	15 (+)	2	3	5	1:5
F2	1	5 (0)	15 (+)	2	3	5	1:5
F3	1	2.5 (-)	15 (+)	2	3	5	1:5
F4	1	10 (+)	10 (0)	2	3	5	1:5
F5	1	5 (0)	10 (0)	2	3	5	1:5
F6	1	2.5 (-)	10 (0)	2	3	5	1:5
F7	1	10 (+)	5 (-)	2	3	5	1:5
F8	1	5 (0)	5 (-)	2	3	5	1:5

Table : 2

Griseofulvin was combined with the solvent solution using a magnetic stirrer set to 1000 revolutions per minute until the drug ingredient was fully dissolved. The polymer was added and stirred until the solution became clear. The plasticizer was added at the end of the lacquer manufacturing process.

C. Physical Characterization of Nail Lacquers

Drying time, water resistance, drug compatibility with excipients, and the ratio of emitted and absorbed heat were all used to assess the quality of nail lacquers. Applying a liquid layer of experimental material on a glass plate and measuring the time until it became dry-to-touch at room temperature (20±2∘C) was used to estimate drying time. The smoothness of the flow was measured by spreading the sample on a glass slide for a long time and then raising it vertically.

Conditions and duration of the micro calorimetric testing		
Temperature ranges	Change speed	Duration
20–100∘ C	1 K/min	4800 s
100–200∘ C	0.5 K/min	12000 s
200–20∘ C	1.2 K/min	9000 s

Table : 3

D. Water resistance

A film (100 L) was distributed uniformly in a 2 x 2 cm2 area on the glass plate and dried at 25 2 °C. After that, the glass plate was weighed and submerged in a 37 °C water bath (HICON, New Delhi, India). After 24 hours, it was removed, cleaned with tissue paper, and reweighed. The weight difference was then determined.

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E. Drying time

On glass petridish, a 4.0 x 4.5 cm2 area was delineated, and a sample film was applied using a nail brush. A stopwatch was used to record the amount of time it took for the film to dry. The readings were taken three times.

F. Viscosity

The viscosity of the improved formulation was determined by Brookfield viscometer R/S-CPS utilisinghelipath spindle #3 at 60 rpm 25 °C using an accurately weighted 100 g of the sample in a beaker.

G. Blush test

The sample (0.2 mL) was uniformly distributed on a glass plate (7.2 × 2.4 cm2) and allowed to dry at room temperature. Ordinary tap water was used to fill a glass beaker (250 mL) halfway. The plate was then submerged in the beaker, resulting in the whole film being submerged in water for 24 hours. The plate was removed, cleaned with tissue paper, and let to dry at room temperature for 4 hours before being examined for blush.

H. Non-volatile content

1 gram of each sample was poured and uniformly distributed on a silicon plate. The dish was precisely weighed before being baked for one hour at 100 degrees Celsius. After that, the plate was withdrawn, cooled, and weighed again. The following equation was used to determine the non-volatile content:

$$Non-volatile\ content = \frac{Final\ weight\ of\ film}{\text{Original weight of film}} X100$$

I. In Vitro Griseofulvin Release Testing

The drug amount diffusing across 1 cm2 cuprophan dialysis membranes (MWCO – 10000 Da) was measured during griseofulvin release studies at 32 C. The diffusion membrane was placed on the diffusion cell, and 50 litres of lacquer experimental formulation was applied evenly over the membrane's surface and left for 4 hours until the lacquer dried completely and a film formed. By calculating weight loss kinetics, a drying time of 4 hours was experimentally shown to be adequate for achieving dry lacquer coating under ambient circumstances. An aluminium foil cover shielded the dry film from the elements. The solubility of griseofulvin in water at 32 degrees Celsius was found to be 950.1 g/mL, and water (15 mL) was utilised as the acceptor phase under sink conditions. To maintain a consistent volume of acceptor liquid, 2 mL of acceptor medium was removed at predetermined time intervals and replaced with the same quantity of new medium. UV spectrophotometry at 294 nm wavelength was used in duplicate to measure the quantity of medication emitted. The quantity of medication released was determined, and the findings were expressed as means SD.

J. Optimization of Compositions

The D-optimal design approach was used to create nail lacquer compositions for optimization based on component quantitative ranges. For each film-forming polymer, eight distinct compositions were created. In vitro release findings were used as the key criterion for optimising experimental nail lacquer formulations.3^2 complete factorial designs were chosen for the manufacture of nail lacquer. There were a total of eight formulations created.

K. In vitro antifungal activity

In vitro antifungal activity towards Candida albicans was determined using the agar cup-plate technique. Autoclaving at 120 oC, 15 pounds pressure for 15 minutes was used to prepare and sanitise nutrient agar plates. After that, a fungus strain, C. albicans, was injected into 30 mL of nutritional agar medium (2 mL of inoculum to 100 mL of nutrient agar media). The liquid was then put onto two sterilisedpetriplates, with three 5 mm diameter wells made in each petriplate using a sterile borer. 0.2 mL of optimal and control formulations were transferred aseptically to the cups and labelled as optimised and control formulations, respectively. Uninoculated medium and media seeded with test organism but without an antifungal agent were used as negative and positive controls, respectively. The prepared petriplates were kept at room temperature for 2 hours to enable the solutions to diffuse into the medium before being incubated at 28°C for 48 hours. The diameter of the zone of inhibition that surrounded each well was measured.

L. Bioadhesivity Studies

One of the most important things to consider while developing an effective transnail medication delivery system for onychomycosis is bioadhesion. Texture Analyzer1 with a 50-kg load cell was used to test the adherence of HPMC lacquer films on cadaver nails.

The TH-loaded or placebo HPMC lacquer was applied to a glass slide that was attached to the Texture Analyzer1's base. On the TA-96 probe, a cadaver nail plate with a diameter of 6 mm was attached. The probe was dropped from a height of 25 mm at 1 mm/s with a force of 3.5 N until the nail plate made contact with the lacquer film's surface. When the nail plate identified the lacquer film's surface, a 0.5 N trigger force was delivered for 30, 60, or 120 seconds. The probe was removed from the surface film at a predetermined speed of 0.5 mm/s after the contact period had expired, and the force needed to remove the nail from the lacquer film was noted as peak adhesive force (PAF). The force deflection profiles were used to calculate the area under the curve (AUC), which reflects the work of adhesion. Both the placebo and drug-loaded lacquer films' two parameters were recorded in triplicate and evaluated.

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M. Resistance to Multiple Washing

A washing method devised and verified in-house was used to test the nail lacquer's capacity to survive repeated washings. Nails were placed on a 0.2 cm2 active diffusion area nail adaptor. In the donor compartment, around 20 mL of drug-loaded hydrophilic nail lacquer was applied to the nail plate.

After the hydrophilic layer had dried completely (approximately 5 minutes), 20 mL of vinyl lacquer was placed on top of the hydrophilic drug-loaded film to create a bilayered film. Approximately 500 mL of distilled water (pH 3.0) was put into the donor compartment after the vinyl film had dried. After allowing the water to stand for 1 minute, it was collected to determine the quantity of TH dissolved. The drug concentration in each washing stage with distilled water was determined, and the total quantity of TH lost from the bilayer lacquer after 50 washings was calculated.

The second series of tests included applying 20 mL of the drug-loaded hydrophilic nail lacquer on its own. The resultant hydrophilic monolayer was washed many times using the same procedure.

The third series of trials was carried out in the same way, but with the addition of a control nail lacquer, and the total quantity of TH lost after repeated washings was determined. The residual quantity of TH contained in the lacquers remained on the nail plate in each instance was also measured by removing the nail plate using the method described previously after exposing the lacquers to repeated washings.

N. Statistical Analysis

SPSS software and Microsoft Office Excel were used to conduct statistical analysis on the experimental data. For correlation analysis, Spearman's rank coefficient was utilised, when the value of P 0.05, a statistically significant difference was found.

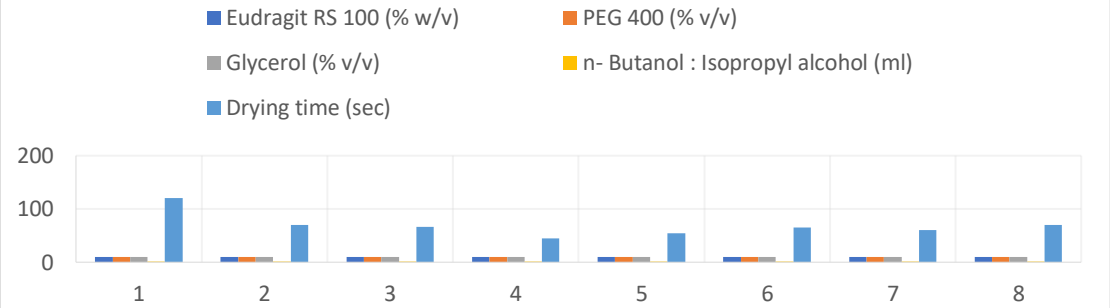
IV. RESULTS

An optimal transungual formulation should need fewer treatments, be simple and comfortable to apply, and have excellent nail adhesion.

Optimization of solvent system

The research was carried out in order to determine the best solvent ratio for nail lacquer formulation. Isopropyl alcohol has a boiling point of 82.4 °C, whereas n-butanol has a boiling point of 117.7 °C. As a result, the assessment was carried out to determine the solvent system (n-butanol and isopropyl alcohol) ratio that can provide the best drying time, with neither too slow nor too rapid evaporation rates. F1 (Graph 4.1), which had the greatest amount of n-butanol, had the fastest drying time of 140 seconds. This was longer than the recommended drying time for a nail lacquer to create a film, which was 1-2 minutes. F4 had the shortest drying time of 36 seconds since it included the least amount of n-butanol and the most amount of isopropyl alcohol. With a total volume of 10 mL and an increased concentration of isopropyl alcohol and a lower percentage of n-butanol, drying time was found to be reduced. In addition, for the production of nail lacquer, a solvent system ratio with an optimal drying time of 60 seconds was chosen.

GRAPH 4.1 -SELECTION OF OPTIMUM RATIO OF DESIRED SOLVENT SYSTEM



A. Preparation and evaluation of nail lacquer

Nail lacquers were tested for drying time, water resistance, non-volatile content, blush test, in vitro adhesion, and antifungal action using a 3^2-factorial design.

B. Characterization of Nail lacquer : Drying time

The time it took for nail lacquer to dry ranged from 53.90 6.42 seconds to 80.46 0.80 seconds (Table 3.) In the instance of nail lacquer, the optimal drying time was discovered to be 1-2 minutes (7). All of the formulations (F1-F9) had drying times within the acceptable range. Formulation F1 with lower levels of TGA and Eudragit RS 100 was determined to have the lowest level of it. The F9 formulation had the longest drying time (80.46 0.80 sec) and the shortest drying time (53.90 6.42 sec).

C. Non-volatile content

Non-volatile content was determined to be in the range of 91.66 0.33 – 98.53 0.36 percent for all nine formulations. Formulation F2 had the highest non-volatile content, while Formulation F1 had the lowest.

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D. Water resistance

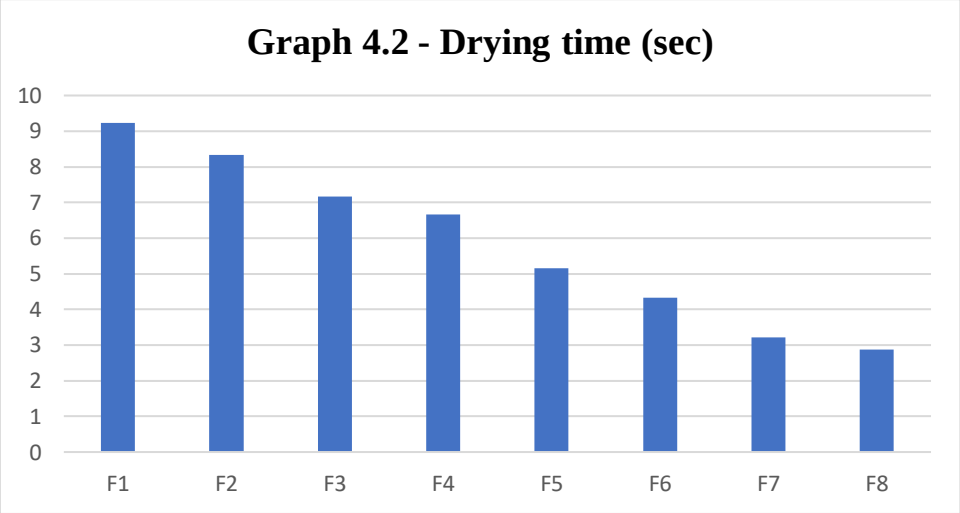
The water resistance of nail lacquer was determined by measuring the weight loss that happened after immersion in water. After 24 hours in water, the quantity of water absorbed by the nail lacquer layer was determined to be reduced. As a result, all of the formulations had a high-water resistance.

E. Blush test

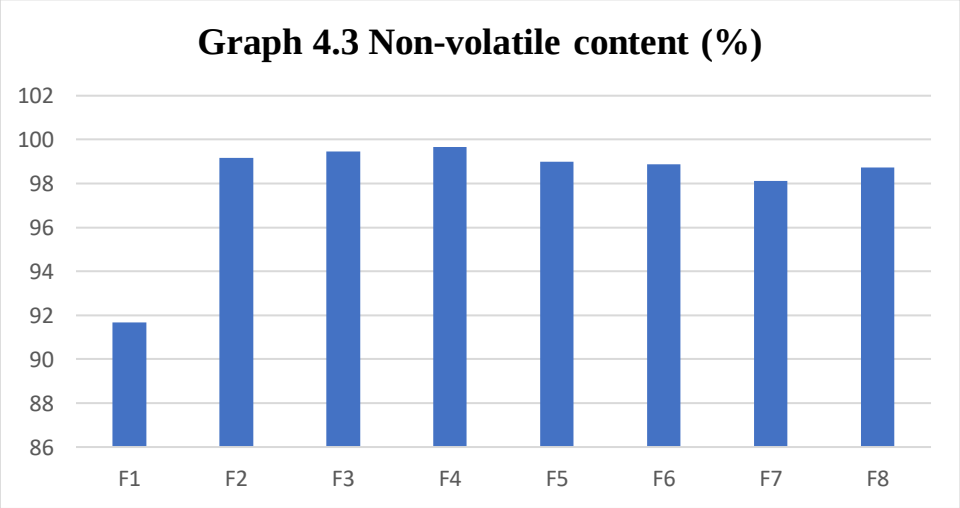
The blush test was passed by all of the formulations. The blush test was allowed since there was no whitishness. Furthermore, no blistering or peeling was seen in any of the formulations.

Characterization of nail lacquer-based formulations of Griseofulvin (F1-F8)				
Formulations	Drying time (sec)	Non-volatile content (%)	Water resistance	Blush test
F1	54.10 ± 5.61	91.67 ± 0.13	High	Pass
F2	62.16 ± 4.66	99.16 ± 0.46	High	Pass
F3	66.61 ± 2.46	99.45 ± 0.91	High	Pass
F4	68.91 ± 5.00	99.67 ± 0.45	High	Pass
F5	70.12 ± 6.44	98.99 ± 0.17	High	Pass
F6	73.21 ± 4.47	98.87 ± 0.71	High	Pass
F7	76.56 ± 1.31	98.11 ± 0.68	High	Pass
F8	79.56 ± 2.83	98.72 ± 0.30	High	Pass

Table : 4



The drying time of formulation F1 was higher while the formulation F8 has least drying time in all formulations.



Formulation F1 has the least non-volatile content while F4 has the highest.

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F. In-vitro release testing

Griseofulvin release time was tested in each formulation with respect to different time intervals. Formulation F8 released 98% of drug within 6 hours.

Table 5 Griseofulvin release rate in all formulations

Time (h)								
Formulation Number								
F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	
26 ± 1.21	35.15 ± 0.55	32.5 ± 0.72	27.9 ± 1.24	27.13 ± 0.6	35 ± 0.78	39.5 ± 1.31	42.8 ± 1.12	**0.25**
36 ± 1.20	46.21 ± 0.61	43.03 ± 0.77	36.9 ± 1.13	33.1 ± 0.9	46.3 ± 0.31	44.5 ± 1.13	51.4 ± 0.90	**0.5**
47.1 ± 1.10	63.12 ± 0.31	54.88 ± 0.96	48.6 ± 1.7	46 ± 0.71	56.2 ± 0.9	54.8 ± 1.24	69.5 ± 0.73	**1**
54.3 ± 1.34	70.17 ± 0.51	57.95 ± 0.61	63.3 ± 1.5	49.1 ± 0.55	67 ± 1.31	66.4 ± 1.43	77 ± 0.85	**2**
59.6 ± 0.99	76.16 ± 0.87	64.67 ± 0.83	73 ± 1.15	53.14 ± 0.66	68.1 ± 0.44	70 ± 1.53	85 ± 0.91	**3**
65.6 ± 1.01	78.93 ± 0.70	68.20 ± 0.53	76 ± 1.2	58.21 ± 0.93	70 ± 0.11	73.4 ± 1.71	95 ± 0.61	**4**
68.7 ± 1.21	82.34 ± 0.61	74.11 ± 0.31	78.1 ± 1.25	62.14 ± 0.41	73 ± 1.21	74.1 ± 1.01	98.1 ± 0.11	**5**
70.8 ± 0.91	89.99 ± 0.63	78.90 ± 0.11	81 ± 1.1	66 ± 0.01	75 ± 1.23	75 ± 1.93	99 ± 1.10	**6**

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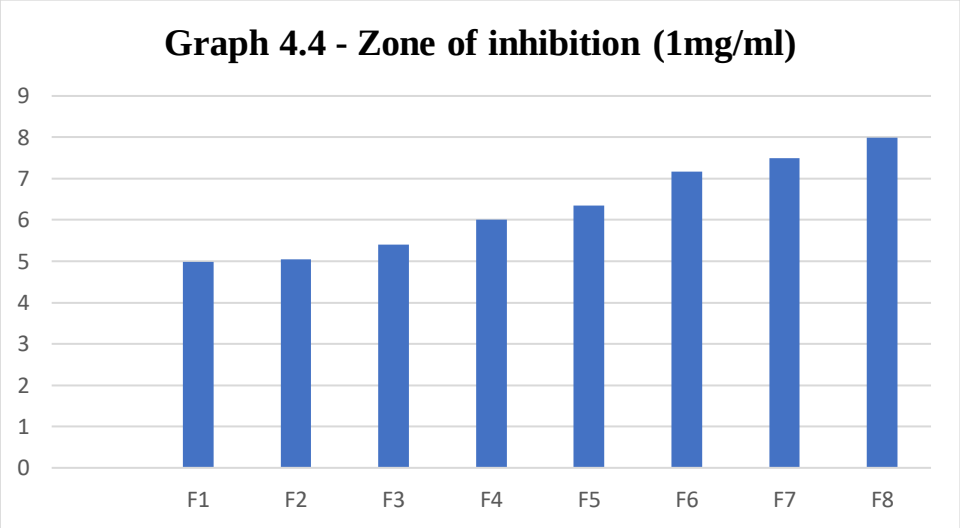
G. In vitro antifungal activity

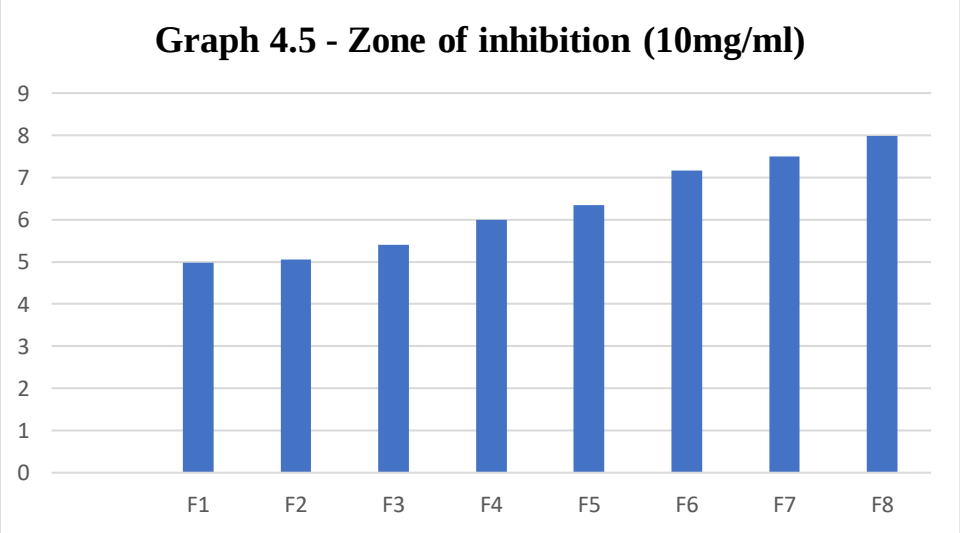
Antifungal efficacy against Candida albicans was tested using a control solution and an improved nail lacquer formulation (F6). Positive and negative controls were also compared (Figures 3A and 3B). When the zone of inhibition was compared, it was discovered that F6 had greater antifungal activity as a higher value of inhibition zone than the control formulation (F6 > CF) (Figure 3C and 3D). The zone of inhibition shown by the optimised formulation was 2.83 0.86 mm, which was determined to be greater than the zone of inhibition shown by the tolnaftate control formulation (1.53 0.61 mm).

Zone of inhibition				
Formulations	Zone of inhibition			MIC
	1mg/ml	10mg/ml	20mg/ml	
F1	4.70 ± 0.30	4.81 ± 0.56	4.98 ± 0.67	800
F2	4.91 ± 0.87	4.99 ± 1.94	5.05 ± 1.01	699
F3	5.16 ± 1.19	5.33 ± 0.43	5.41 ± 0.87	760
F4	5.66 ± 0.45	5.91 ± 0.50	6.00 ± 0.87	810
F5	6.01 ± 0.73	6.07 ± 0.76	6.34 ± 0.86	790
F6	6.51 ± 1.91	6.78 ± 0.93	7.17 ± 1.31	789
F7	7.13 ± 1.19	7.41 ± 1.13	7.5 ± 0.71	663
F8	7.76 ± 0.37	7.93 ± 0.16	7.99 ± 0.13	812

Table : 6



Formulation F8 showed greater zone of inhibition in 1mg/ml as compared to others.



With 10mg/ml formulation F8 showed greater zone of inhibition and F1 and F2 showed equal zone of inhibition.

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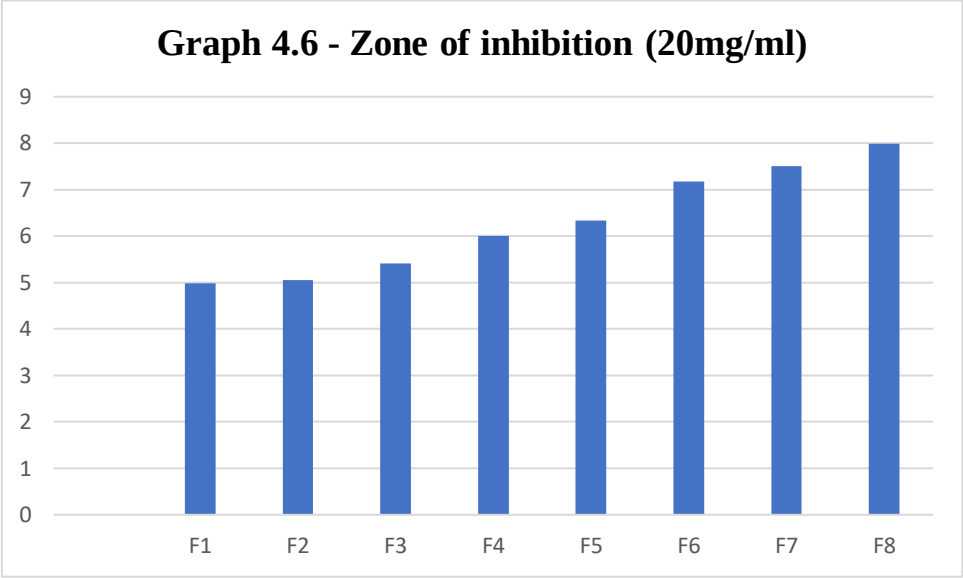
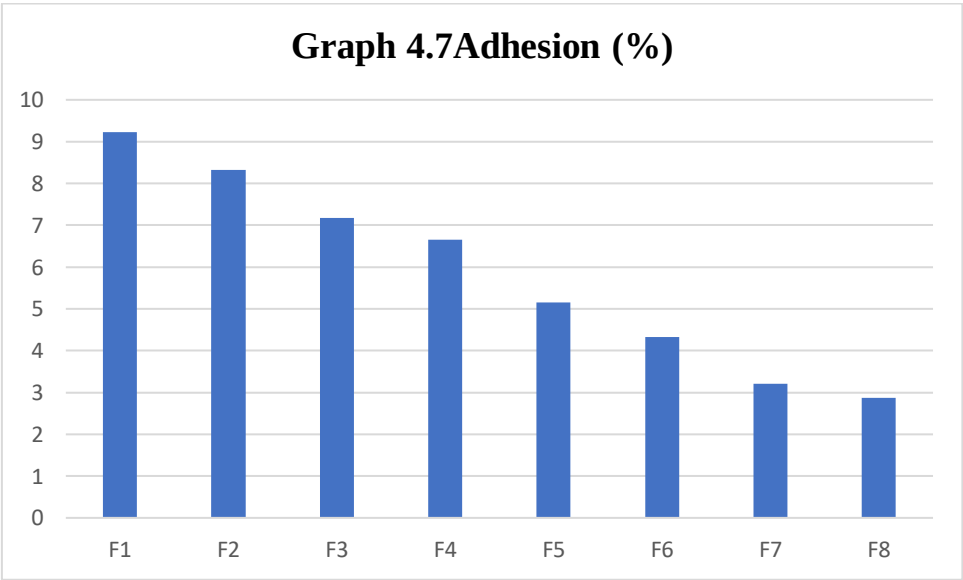


With 20mg/ml, Formulation F8 showed greater zone of inhibition.

H. Bio adhesivity

Bio adhesivity	
Formulations	Adhesion (%)
F1	9.23
F2	8.33
F3	7.17
F4	6.66
F5	5.15
F6	4.33
F7	3.21
F8	2.87

Table : 7



Bio adhesion of formulation F1 was greater as compared to other formulations. F8 showed minimum bio adhesion with respect to other formulations.

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V. DISCUSSION AND CONCLUSION

Onychomycosis is a fungal infection that causes thickness, discolouration, and detachment of the finger or toenails from the nail bed. Medication transfer through the nail to provide targeted drug administration in order to cure nail disorders is known as transungual drug delivery. Because of its superior adherence and localised action, which offers less systemic adverse effects, the transungual medication delivery method is considered to be highly useful in managing nail diseases [97]. Ungual treatment has many advantages over oral/systemic medication administration, including ease of preparation compared to oral dose forms such as pills, and so on. It improves adherence and is appropriate for individuals who cannot take systemic medicine [98].

Nail lacquers have long been used as a cosmetic to preserve and beautify the nails. Medicated nail lacquers are a novel kind of formulation that has been utilised to administer drugs transungally [99]. Solvent evaporation occurs when the product is applied to the nail plate. After the solvent has evaporated, the film left behind acts as a drug depot. The medication is released and penetrated throughout the nail for an optimal time period from this drug shop. For drug penetration into the nail plate, a high diffusion gradient is created [100].

The bilayered nail lacquer was created with the specific goals of:

- maximising the adhesion of the drug loaded lacquer film to the nail surface using a hydrophilic bio-adhesive polymer,
- retaining the supersaturated hydrophilic lacquer film on the nail plate for a long time using a durable water-resistant hydrophobic layer, and
- ensuring delivery of effective amounts

Aqueous-based nail lacquers are known to enhance nail hydration and medication diffusion over the nail plate, and therefore play an important role in onychomycosis therapy. Because the nail plate is known to act like a hydrogel when wet, the hydrophilic lacquer layer should adhere better to the curves of the nail plate. Furthermore, when applied to the extremely delicate nail bed, water-based nail lacquers do not cause a burning sensation. Because it produces a non-sticky, nonglossy bioadhesive film with excellent flexibility, hydroxypropyl methylcellulose was chosen as the film forming [101].

Water loss from the surface of the nail plate into the environment is also reduced as a result of the development of a film on the nail plate. Hyperhydration of the top nail plate layers occurs, which aids drug diffusion even more. Penetration enhancers such as hydration agents, keratolytic agents, and thiol compounds may further improve active agent penetration.

The current study used a 3^2 factorial design to create nail lacquer-based formulations. The non-volatile content, drying time, blush test, water resistance, and in vitro adhesion study of all the produced formulations were then investigated. The drying time of newly designed nail lacquers was regarded an essential criterion. As previously stated, a short drying period results in poor lacquer flow. As a consequence, the film will be uneven and streaky, and it will be boring. Furthermore, the sample's residence duration on the nail lacquer brush will be decreased, making nail lacquer application on the nail plate more difficult. An excessively long drying period may cause hardening of nail lacquer and poor pick-up of the lacquer on the brush. As a result, having an optimal drying period of 1-2 minutes is deemed ideal.

All of the values were found to be within the stated optimal range after drying time analysis. The quantity of coverage that the nail lacquer may achieve is determined by determining the non-volatile component. The solvent in the formulation evaporates, leaving behind solid components that give coverage for the whole nail plate. The concentration of polymer utilised determines the non-volatile content, which was shown to be exactly proportional to the concentration of Eudragit. Because of the greatest concentration of Eudragit RS 100, Formulation F4 had the largest non-volatile content.

A water resistance test was used to evaluate the water resistance of nail lacquer. Weight loss may occur as a result of water absorption followed by surface erosion from the film, depending on the solubility of the film in the medium. Eudragit RS 100 aids in the development of a water insoluble film, which results in no or little weight loss. The blush test was used to track physical changes in the nail lacquer layer, such as blistering or peeling, when it was exposed to water or the outside environment. All of the formulas had the best shine and stayed that way even after the test. Apart from these qualities, nail lacquer must stick effectively to the nail plate in order to create a film over it. As a result, excellent adhesive properties are needed. An in vitro adhesion research was conducted to verify this. Eudragit-prepared films had the best adhesive qualities. When a result, the % peel off of film was found to decrease as the concentration of Eudragit was raised. The impact of TGA on film strength, on the other hand, was shown to be negligible.

In phosphate buffer, pH 7.4, the quantity of medication penetrated per unit area per unit time (flux) utilising bovine hoof membrane was measured. All formulations have similar amount of Eudragit RS 100. TGA is a thiolic molecule with a sulphydryl group (-SH) that is responsible for the disulphide bond cleavage in nail keratin. Thioglycolic acid's impact was ascribed to its tiny molecular weight and the keratin network disruption it produced. It causes a decrease in the lipid content of the dorsal nail layer, causing the nail structure to be disrupted (29). TGA was shown to be efficient as a permeation enhancer in moving tolnaftate across the experimental membrane because to the presence of disulfide linkages in bovine foot. Furthermore, in the case of formulations that achieve successful permeation, target flow is regarded an essential metric in assessing permeation effectiveness. The minimal flux needed by the medication to permeate through the semi-permeable membrane in order to have the best therapeutic effect is known as target flux.

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All of the formulations' experimental flux values were found to be higher than the necessary target flux, suggesting that they can reach therapeutic levels. In order to verify the design, an additional design check point formulation was created. The design was verified when there was a small difference between anticipated and observed values. After that, Formulation F6 was chosen as the best formulation and tested for antifungal efficacy, stability, and viscosity. Desirable viscosity had a key effect in preventing drug penetration through the nail lacquer.

Onychomycosis is a fungal illness that mainly affects the finger and toe nails. It is estimated that it affects approximately 19 percent of the world's population and accounts for nearly half of all nail disorders. It's often dismissed as a minor condition with mainly aesthetic consequences, yet it may cause shame and lower self-esteem. It may cause pain and spread to adjacent tissues if not treated properly. It is a common nail condition caused by non-dermatophyte, moulds and dermatophytes. Onychomycosis is thought to be caused by non-dermatophyte filamentous fungus. Because of a variety of cultural and socioeconomic variables, the prevalence of this illness may vary across the world.

Antifungal formulations for translingual drug administration are complicated systems affected by the solubility of the polymers employed, plasticizers, and the medication's physicochemical properties. Before and after film drying, the system of evaporating solvents employed in lacquer formulation should guarantee dissolution of formulation components and creation of a homogenous result. The use of appropriate quality testing techniques offers accurate information on potential lacquer system component interactions as well as biopharmaceutical characterization of the drug-containing film.

The capacity to evaluate the appropriateness of tested polymers for formulation of nail lacquers was shown via testing of water resistance, drying time, compatibility tests, microcalorimetric analysis, and in vitro release testing. The findings supported the use of Eudragit RS100 and Eudragit RL100 for future lacquer composition optimization research. In vitro biopharmaceutical testing verified the acceptability of proposed formulations, and optimization led in the determination of quantitative composition of nail lacquers comprising both Eudragit RL100 and Eudragit RS100 as film-forming polymers. Formulation F8 showed greater anti-fungal activity and in-vitro drug releasing as compared to other formulations while formulation F1 showed greater bio-adhesion.

The use of optimization technologies to develop and find griseofulvin lacquer formulations with specified quality criteria proven to be a useful technique. Transungual griseofulvin delivery studies should be used to validate the quality of improved nail lacquer formulations.

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